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EXAMINER: GUZO, D

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This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☑ This application has been examined ☑ Responsive to communication filed on 6/10/92 ☐ This action is made final.

A shortened statutory period for response to this action is set to expire three (3) month(s), ~~days~~ from the date of this letter. Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☑ Notice of References Cited by Examiner, PTO-892.
2. ☐ Notice re Patent Drawing, PTO-948.
3. ☑ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, Form PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____

Part II SUMMARY OF ACTION

1. ☑ Claims 39-60 are pending in the application.
   Of the above, claims 48 and 49 are withdrawn from consideration.
2. ☐ Claims _____ have been cancelled.
3. ☐ Claims _____ are allowed.
4. ☑ Claims 39-47 and 50-60 are rejected.
5. ☐ Claims _____ are objected to.
6. ☐ Claims _____ are subject to restriction or election requirement.
7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable. ☐ not acceptable (see explanation or Notice re Patent Drawing, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____ has (have) been ☐ approved by the examiner. ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed on _____, has been ☐ approved. ☐ disapproved (see explanation).
12. ☑ Acknowledgment is made of the claim for priority under U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☑ been filed in parent application, serial no. 07/117071; filed on 10/23/87
13. ☐ Since this application appears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

EXAMINER'S ACTION

PTOL-326 (Rev. 9-89)

Applicant's election with traverse of Group 1 in Paper No. 6 is acknowledged. The traversal is on the ground(s) that a search of both inventions would not entail a serious burden on the part of the examiner. This is not found persuasive because a proper search of the two inventions would require, in addition to the search for Group I, a search of the DNA hybridization art, vector art, tissue cell culture art, diagnostic disease detection art, art related to use of DNA probes in disease detection and art related to disease conditions associated with altered metabolic enzyme (e.g. GS) levels. It must be considered that a serious search burden would exist in the absence of a restriction between the two inventions.

The requirement is still deemed proper and is therefore made FINAL.

Claims 48 and 49 are withdrawn from further consideration by the examiner, 37 C.F.R. § 1.142(b), as being drawn to a non-elected invention, the requirement having been traversed in Paper No. 6.

35 U.S.C. § 101 reads as follows:
"Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title".

Claims 47 and 56 are rejected under 35 U.S.C. § 101 because the claimed invention is drawn to non-statutory subject matter.

The fragment of genomic DNA recited in Claim 47 could be interpreted, in its broadest sense, to encompass an entire naturally occuring genomic DNA molecule or chromosome and therefore the claim reads on a product of nature.

It is noted that Claim 56, as drafted, reads on a "Use of a vector..." and therefore does not fall within any of the recognized categories of patentable inventions (See also 35 USC 100).

The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office

action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

Claims 39-47, 50, 51 and 55 are rejected under 35 U.S.C. § 103 as being unpatentable over Sanders et al. in view of Alberts et al. or Watson et al.

Applicants recite a recombinant DNA sequence encoding the amino acid sequence of a hamster glutamine synthetase (GS) enzyme, a recombinant expression vector containing said GS sequence and a host cell transformed with said sequence.

Sanders et al. (AR, EMBO, Vol. 3, 1984, pp. 65-71, See whole document, particularly p. 69) recite the cloning of at least part of the hamster GS gene. Sanders et al. do not recite generation

of an expression vector capable of expressing the GS gene or host cells transformed with said gene.

ALberts et al. ("Molecular Biology of the Cell", 1983, pp. 184-193) and Watson et al. ("Recombinant DNA, A Short Course", 1983, pp. 184-193) recite the generally routine steps of cloning a gene and expressing a cloned gene of interest in transformed host cells.

Applicants invention is essentially a logical conclusion to the work of Sanders et al. Applicants indeed recite that the methods used by Sanders et al. were duplicated in the instant disclosure (See Specification, Page 17, 2nd paragraph); therefore, given the teachings on preliminary identification of a portion of the GS gene (Sanders et al.) it must be considered that the subsequent cloning, sequencing and expression of the entire GS gene by following of the routine cloning and expression steps outlined by Alberts et al. and Watson et al. would have been obvious to an artisan of ordinary skill in the art. An ordinary skilled artisan, seeking to isolate, clone and express an amplifiable gene, such as the GS gene, for potential use in coamplifying an additional foreign gene of interest, would have been motivated to use the teachings of Sanders et al. on a preliminary characterization and cloning of at least part of the GS gene combined with the routine steps of cloning, sequencing and expressing genes of interest in microorganisms recited by Alberts et al. and Watson et al. in order to isolate, clone and

express the GS gene.

Claims 52-54 and 56-60 are rejected under 35 U.S.C. § 103 as being unpatentable over Sanders et al. in view of Alberts et al. or Watson et al. all further in view of Axel et al. (AA).

Applicants recite the use of a recombinant DNA vector comprising the amplifiable marker GS gene sequence and further comprising a second DNA sequence encoding a non-GS protein of interest, with said genes linked so as to result in amplification of the non-GS coding sequence. Applicants further recite the specific plasmids comprising the GS and tPA genes (pSVLGS.tPA16 and pSVLGS.tPA17), and use of recombinant plasmids comprising the GS gene to confer survivability to cells lacking adequate GS activity.

Sanders et al., Alberts et al. and Watson et al. are applied as above. Sanders et al., Alberts et al. and Watson et al. do not teach co-amplification of two different linked or un-linked DNAs.

Axel et al. (AA, U.S. Patent # 4399216, 8/16/83, See whole document, particularly the abstract and Column 3, 1st paragraph of "Summary" section, Column 5, last 2 paragraphs and Claim 54) recite the co-amplification of two different linked or un-linked DNAs, one DNA being an amplifiable gene coding for a dominant selectable marker such as drug resistance and the second DNA being a gene coding for a protein of interest.

Applicants invention is essentially an obvious variation on

the teachings disclosed by Axel et al. It is noted that Axel et al. recite the linking, in a plasmid vector, of a dominant amplifiable, selectable, gene with a cloned gene of interest and the selection conditions for identification of cells which have acquired, amplified and expressed the selectable phenotype and hence the second cloned gene of interest. Therefore, an ordinary skilled artisan, seeking to amplify and express a gene of interest (e.g. tPA) by linking said gene to a dominant, amplifiable, selectable gene would have been motivated to use the teachings of Sanders et al. on the partial identification and cloning of the amplifiable dominant selectable GS gene combined with the teachings of Alberts et al. and Watson et al. on the routine steps involved in cloning, sequencing and expressing a gene of interest further combined with the teachings of Axel et al. on a method of amplifing and expressing a gene of interest by linking said gene to a dominant selectable gene (the GS gene would fall into this category) and selecting for cells containing the two amplified genes under conditions suitable for survival of the cells containing the amplified dominant selectable gene in order to generate a recombinant vector with the dominant selectable amplifiable gene (GS) linked to a second gene of interest, transform suitable host cells (i.e. CHO-K1 cells) and culture cells under conditions which would permit selection of cells carrying the amplified genes. It would have been obvious to an ordinary skilled artisan, endeavoring to develope a

procedure for amplification and expression of a gene of interest to use the teachings of Sanders et al. on the partial characterization of an amplifiable dominant selectable gene (GS) combined with the teachings of Alberts et al. and Watson et al. on the routine steps necessary to successfully clone, sequence and express a gene of interest further combined with the teachings of Axel et al. on the amplification and expression of genes of interest by linking said genes to amplifiable and selectable genes (e.g. GS) and selection of said gene combinations by culturing the transformed cells under selective conditions permitting survival of the cells which have acquired the gene combination in order to generate expression vectors (and transformed cells) comprising the GS gene and a gene encoding a protein of interest and culturing said transformed cells under conditions allowing for amplification and expression of said gene combinations.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to provide an adequate written description of the invention.

The plasmids pSLGS.tPA16 and pSVLGS.tPA17 are necessary for practicing of the instant invention in that these recombinant plasmids contain the DNA sequences coding for the GS gene, a foreign gene (tPA) and the sequences necessary for expression and/or amplification of said DNA. Given that the plasmids are essential for enablement of the invention and have not been described in sufficient detail to enable one of ordinary skill in the art to exactly duplicate said plasmids, a deposit of said plasmids is deemed necessary (See attachment on "Deposits of Biological Materials").

Claims 53 and 54 are rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth in the objection to the specification.

Claims 39 and 40 are rejected under 35 U.S.C. § 112, first paragraph, as the disclosure is enabling only for claims limited to a hamster GS gene. See M.P.E.P. §§ 706.03(n) and 706.03(z). Applicants recite claims to recombinant DNA sequences encoding mammalian or rodent GS genes but have enabled only the hamster GS gene and have not recited how one of ordinary skill in the art would go about isolating and identifying GS genes from any or all possible mammalian or rodent species. To identify GS genes from any mammal or rodent species it would be necessary to derive cell lines from that species (if they can be derived), select for mutants defective in GS activity (if they can be generated), isolate the regions of heterogeneity in the mutant and normal

cell lines, fine map the sequences of interest, and finally determine if they encode a GS gene. Given these steps and the uncertainties inherent in each step, it is considered that undue experimentation would be required to practice the instant invention.

Claims 57 and 59 are rejected under 35 U.S.C. § 112, first paragraph, as the disclosure is enabling only for claims limited to CHO-KI myeloma cells. See M.P.E.P. §§ 706.03(n) and 706.03(z).

It is unclear if myeloma cell lines can be generated from all mammalian species (Claim 57) or from any animal species (Claim 59). To practice the instant invention, an ordinary skilled artisan would need to generate myeloma cell lines from any animal or mammal species of interest. Given that myeloma cell lines have been isolated from only a few of the thousands of potential animal species in question, given the extensive diagnostic, clinical procedures and in vitro cell culture techniques involved in identification, characterization, cloning and maintaining a new myeloma cell line and given that myeloma cell lines may not be able to be generated from all mammalian or animal species, it is considered that undue experimentation would be required to practice the instant invention.

Claims 44, 56, 57, 58 and 59 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter

which applicant regards as the invention. Claim 44 is indefinite in that it is unclear what "high stringency conditions" encompasses, it is unclear what "mammalian species" applicants are referring to and it is unclear what DNA sequence comprises "a part thereof from a different species". Claim 56 is indefinite in that a method claim must be drafted in terms of specific method or process steps. Mere recitation of the "use of" an invention is not acceptable claim language. As Claims 57-59 are dependent on Claim 56, they also are rendered indefinite.

Any inquiry concerning this communication should be directed to David Guzo at telephone number (703) 308-1906.

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SUPERVISORY PATENT EXAMINER
ART UNIT 185